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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/850,041	05/07/2001	Attila Lorincz	2629-4023	1436

7590 06/07/2002
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EXAMINER

MYERS, CARLA J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 06/07/2002

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/850,041

Applicant(s)

LORINCZ ET AL.

Examiner

Joseph Weitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2002.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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1. This action is in response to Paper No. 6, filed March 13, 2002. Applicants arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are withdrawn. This action is made FINAL.

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,228,578. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '578 are both drawn to non-radioactive hybridization assays which comprise the steps of hybridizing a nucleic acid that has been hydrolyzed with base to a probe to form a double-stranded DNA/RNA hybrid; capturing the hybrid onto a solid phase to which an anti-RNA/DNA antibody has been immobilized; eliminating non-hybridized probe, particularly by nuclease digestion; and detecting bound DNA/RNA hybrids. Furthermore, the instant claims and the claims of '578 are both inclusive of kits comprising a transport medium, a probe, a solid phase to which an anti-RNA/DNA antibody is immobilized and a means for detecting DNA/RNA hybrids.

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In the response of Paper No. 6, Applicants state that the rejection has been overcome by the filing of a terminal disclaimer over U.S. Patent 6,228,578. However, the application/patent being disclaimed has been improperly identified since the number used to identify the patent being disclaimed is incorrect. The correct number is 6,228,578, not U.S. Patent 5,981,179, as set forth in the terminal disclaimer.

THE FOLLOWING INCLUDES NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

3. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the embodiment of "unmodified" probes. While the specification teaches labeled and unlabeled probes, the specification does not define, nor teach the concept of, "unmodified" probes.

4. Claims ³³~~34~~ and 43-45 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim ³³~~34~~ is indefinite over the recitation of "unmodified probes". The specification does not provide a definition for this phrase and there is no art recognized definition for what constitutes an unmodified probe. It is unclear as to whether this is intended to refer to, for example, unlabeled

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probes, probes which are not protected at their terminus, or probes which are isolated from nature (versus, chemically synthesized probes).

Claims 43-45 are indefinite over the recitations of "probe comprises HPV 6 and HPV 11" (claim 43), "probe comprises HPV 16..." (claim 44) and "probe contains one or more HPV types" (claim 44) because it is unclear as to whether the probe contains full genomic copies of the stated HPV types and if the probe includes copies of each of the HPV types (i.e., for claim 44 does the probe contain a copy of each of the genomes of HPV 16, 18, 31, 33 and 35?). Clarification of the claims is required.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

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Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rashtchian.

Rashtchian (page 1527) teaches a non-radioactive hybridization assay comprising (a) treating a cell sample with sodium hydroxide lysis solution to generate a “hydrolyzed sample of cells”; (b) contacting the hydrolyzed sample of cells with a DNA probe to form a double-stranded RNA/DNA hybrid between the DNA probe and target RNA; c) capturing the RNA/DNA hybrid onto a solid phase using an immobilized antibody specific for the hybrid; (d) washing to remove unhybridized probe; and (e) detecting the bound hybrid as indicative of the presence of the target RNA. The bound hybrids are detected using a streptavidin-peroxidase reagent. The method of Rashtchian requires the use of the reagents of buffers, which can be used to stabilize biological samples, a DNA probe, a solid support to which an anti-RNA/DNA antibody has been immobilized, and a streptavidin-peroxidase reagent for detecting bound RNA/DNA hybrids. Rashtchian does not teach packaging these reagents into a kit. However, reagent kits for performing diagnostic methods were conventional in the field of molecular biology at the time the invention was made. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents of a buffer, a DNA probe, a solid-support having an anti-RNA/DNA antibody immobilized thereon, and a detection means in a kit for the expected benefits of convenience and cost-effectiveness for practioners in the art wishing to perform the detection method of Rashtchian.

In the response of Paper No. 6, Applicants traverse this rejection by stating that Rashtchian teaches use of a biotinylated probe, but does not teach use of an unmodified probe. This argument

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is not convincing because, as discussed above, it is unclear as to what is intended to be encompassed by an unmodified probe. Unmodified with respect to what property of the probe? Since it is unclear as to what constitutes an unmodified probe, the biotinylated probe of Rashtchian is considered to be included by the claimed invention. Applicants further argue that there is no motivation to modify the probe of Rashtchian so that it is directed against another target nucleic acid. However, the claims are drawn broadly to include probes to any target nucleic acid. Accordingly, there is no requirement to modify the probe of Rashtchian to meet the limitations of the claim. Applicants also argue that the method of Rashtchian does not require a sample transport medium for stabilization of the sample. However, the method of Rashtchian does require the use of a buffer. It is well known and accepted in the art that buffers allow for the stabilization of samples. Accordingly, it is a property of the buffer of Rashtchian that it constitutes a medium for stabilization of samples.

6. Claims 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rashtchian in view of Carrico (U.S. Patent No. 5,200,313).

Rashtchian (page 1527) teaches a non-radioactive hybridization assay comprising (a) treating a cell sample with sodium hydroxide lysis solution to generate a "hydrolyzed sample of cells"; (b) contacting the hydrolyzed sample of cells with a DNA probe to form a double-stranded RNA/DNA hybrid between the DNA probe and target RNA; c) capturing the RNA/DNA hybrid onto a solid phase using an immobilized antibody specific for the hybrid; (d) washing to remove unhybridized probe; and (e) detecting the bound hybrid as indicative of the presence of the target RNA. Rashtchian teaches labeling the probe with biotin and detecting immobilized/bound probe using a

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streptavidin-peroxidase complex. Rashtchian does not teach using an unlabeled probe or detecting the immobilized probe using an antibody reactive with the RNA/DNA hybrid.

Carrico (col. 2-3) teaches a method for detecting a target nucleic acid wherein the method comprises detecting an immobilized RNA/DNA hybrid using an antibody that specifically reacts with the hybrid. The reference further teaches detecting the antibody bound to the immobilized RNA/DNA complex using a labeled anti-(antibody) antibody. The reference also teaches that the anti-hybrid antibody may be labeled and detected directly (column 10).

In view of the teachings of Carrico, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Rashtchian so as to have detected the immobilized RNA/DNA hybrid using an antibody reactive with the RNA/DNA hybrid in order to have achieved the benefits stated by Carrico of obviating the need to label the probe, thereby providing a simpler and more convenient detection method.

With respect to claim 33, modification of the method of Rashtchian as discussed above results in an assay that requires the reagents of buffers, which can be used to stabilize biological samples, an unlabeled/ "unmodified" DNA probe, a solid support to which an anti-RNA/DNA antibody has been immobilized, and a means for detecting bound RNA/DNA hybrids. Rashtchian does not teach packaging these reagents into a kit. However, reagent kits for performing diagnostic methods were conventional in the field of molecular biology at the time the invention was made. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents of a buffer, a unlabeled/ "unmodified" DNA

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probe, a solid-support having an anti-RNA/DNA antibody immobilized thereon, and a detection means in a kit for the expected benefits of convenience and cost-effectiveness for practioners in the art wishing to perform the detection method of Rashtchian.

7. Claims 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rashtchian in view of Carrico and further in view of Thompson.

The teachings of Rashtchian and Carrico are presented above. In particular, Rashtchian teaches removing unhybridized probe by performing repeated wash steps but does not teach using an enzyme, such as RNase, to remove unhybridized probe.

However, Thompson et al. (p. 264, column 2) discloses a hybridization assay wherein unhybridized RNA probe is removed from the reaction mixture by treatment with RNase. Thompson (p. 264) states that "in solution hybridization, unreacted probe is usually in vast excess over hybrids. This creates the problem of a background signal arising from non-specific interaction of probe with solid supports used to purify hybrids. Background signals usually determine the sensitivity of an assay. Three general strategies have been employed to accomplish hybrid purification: selective immobilization, nuclease digestion of unhybridized probe, and sandwich hybridization". In view of the disclosure of Thompson, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Rashtchian so as to have included the step of RNase digestion taught by Thompson for the advantage expressly stated by Thompson of more efficiently removing unhybridized probe, thereby reducing background signal and increasing the overall sensitivity of the detection method.

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Secondly, Rashtchian does not teach methods in which 1-500 ng/ml, particularly 75 ng/ml is utilized. However, to determine the optimum concentration of reactants is well within the skill of the art (see In re Kronig 190 U.S.P.Q. 425). Furthermore, Thompson (page 264) teaches that solution hybridization methods should be performed using excess probe. As stated by Thompson, “under these conditions, all targets in a sample can be saturated with probe. The rate of the reaction is dependent upon the concentration of probe, and independent of target concentration, so that all reactions are complete at the same time, regardless of the amount of target present”. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made and well within the skill of the art to have selected and used an effective amount of probe based upon the specific reaction conditions for each sample for the expected benefit of optimizing the effectiveness and sensitivity of the non-radioactive hybridization method.

8. Claims 41, 42, 46, 47, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rashtchian in view of Carrico and further in view of Longiaru (U.S. Patent No. 5,232,829).

The teachings of Rashtchian and Carrico are presented above. In particular, Rashtchian teaches a method for detecting *Campylobacter* but does not teach applying this method to the detection of HPV, HBV or Chlamydia. However, one of ordinary skill in the art would readily recognize that a nucleic acid technique which detects the presence of a sample nucleic acid via the use of a probe could be applied to the detection of any target nucleic acid and thereby would recognize that the method of Rashtchian would be applicable to the detection of any desired target nucleic acid. Furthermore, Carrico teaches that the method disclosed therein of detecting an

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immobilized probe/target nucleic acid complex with an antibody directed against RNA/DNA hybrids is useful for the detection of any viral or bacterial target sequence (see column 1). Additionally, Longiaru teaches methods for detecting a target nucleic acid and discusses the need to develop assays for the detection of HPV, HBV and chlamydia (see columns 9-10).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Rashtchian in view of Carrico to the detection of HPV, HBV and chlamydia in order to have developed an effective and sensitive means for detecting the presence of these organisms. Moreover, reagent kits for performing diagnostic methods were conventional in the field of molecular biology at the time the invention was made. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents of a buffer, a probe complementary to HPV, HBV or chlamydia nucleic acids, a solid-support having an anti-RNA/DNA antibody immobilized thereon, and a detection means in a kit for the expected benefits of convenience and cost-effectiveness for practitioners in the art wishing to perform the detection method of Rashtchian and wishing to detect the presence of HPV, HBV, or Chlamydia.

9. Claims 41-45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rashtchian in view of Carrico and further in view of Herzog (U.S. Patent No. 4,983,728).

The teachings of Rashtchian and Carrico are presented above. In particular, Rashtchian teaches a method for detecting *Campylobacter* but does not teach applying this method to the detection of HPV, particularly HPV 6, 11, 18, 31, 33, 35, 42, 43 or 44. However, one of ordinary

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skill in the art would readily recognize that a nucleic acid technique which detects the presence of a sample nucleic acid via the use of a probe could be applied to the detection of any target nucleic acid and thereby would recognize that the method of Rashtchian would be applicable to the detection of any desired target nucleic acid. Furthermore, Carrico teaches that the method disclosed therein of detecting an immobilized probe/target nucleic acid complex with an antibody directed against RNA/DNA hybrids is useful for the detection of any viral or bacterial target sequence (see column 1). Additionally, Herzog teaches methods for detecting a target HPV nucleic acid and discusses the need to develop assays for the detection of HPV 6, 11, 16, 18 and 33 (see columns 1 and 2).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Rashtchian in view of Carrico to the detection of HPV 6, 11, 16, 18 and 33 in order to have developed an effective and sensitive means for detecting the presence of these HPV types. Moreover, reagent kits for performing diagnostic methods were conventional in the field of molecular biology at the time the invention was made. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents of a buffer, a probe complementary to HPV 6, 11, 16, 18 or 33 nucleic acids, a solid-support having an anti-RNA/DNA antibody immobilized thereon, and a detection means in a kit for the expected benefits of convenience and cost-effectiveness for practitioners in the art wishing to perform the detection method of Rashtchian and wishing to detect the presence of HPV 6, 11, 16, 18 or 33.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

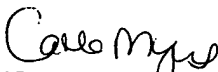
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers


CARLA J. MYERS
PRIMARY EXAMINER

June 2, 2002